

Tuberculosis – a missed opportunity?

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ABSTRACT – The recent publicity surrounding tuberculosis (TB) in both the medical and the lay press, particularly in reference to a number of outbreaks of the disease in British schools, is a timely reminder of a ‘forgotten’ disease that has never really gone away. Following a marked decrease in notification rates in developed countries in the 1960s and 1970s, TB control and treatment programmes were downgraded in the West, and soon both medical professionals and the lay public ceased to be able to identify early symptoms of the infection. Meanwhile, poorer countries continued to struggle to provide even basic medical resources, and death and sickness from TB continued unchecked. More recently, however, there has been a rise in the number of new cases of TB in industrialised nations, together with the emergence of multi-drug-resistant strains of the bacillus. This article reviews these and other aspects of the effectiveness of both UK and international TB control programmes.

KEY WORDS: tuberculosis (TB), multi-drug-resistant tuberculosis (MDR TB), active disease, infection, national TB programme, professional awareness, public awareness, stigma, directly observed therapy (DOTS), costs

The recent so-called ‘outbreaks’ of tuberculosis (TB) in a college in Leicester, a school in Newport and a nursery school in Wandsworth, London, have highlighted the virulent capacity of an infection for which a cure was discovered nearly half a century ago¹. Tuberculosis, particularly in Westernised countries, had, until recently, become a forgotten disease. On a par in the layman’s mind with smallpox, it had been banished to the scientist’s laboratory, never again to trouble us with its presence.

If we had, along with improvements in sanitation, nutrition and general living standards, taken the proverbial bull by the horns and promoted a structured well-organised worldwide TB treatment programme, would we still be in the position where one-third of the world’s population is infected with TB and where 2–3 million people die of the disease each year^{2–5}? Did we, in fact, get tantalisingly close to eradicating the disease, or is that just wishful thinking?

Notification rates for TB have increased in the UK over the last 10 years, and the latest problems in this country, together with outbreaks such as the New York multi-drug-resistant TB (MDR TB) epidemic in the late 1980s, have highlighted the inadequacy of TB control and education programmes even in developed nations^{6,7}. We need to clarify and broadcast the definitions of ‘infection’ and ‘active disease’, raise medical and public awareness of the disease, and stress the importance of funding adequate control programmes and providing well-trained staff.

TB: problems with terminology

The terms ‘tuberculous infection’ and ‘tuberculous disease’ may be a cause of confusion. While one-third of the world’s population is ‘infected’ with the tuberculosis bacterium, they do not all have ‘active’ symptomatic tuberculosis. Bacilli may lie dormant for many years, and the lifetime risk of infected individuals developing active disease is about 10%. This figure rises steeply in those who are immunocompromised, particularly by the HIV virus, with a yearly risk of developing active disease of 10%^{8,9}.

There is also confusion between ‘smear-positive’ and ‘smear-negative’ disease, as well as between ‘open’ and ‘closed’ TB. ‘Smear-positive’ or ‘open’ disease refers to pulmonary TB in which acid-fast bacilli (AFBs) can be seen on light microscopy of the sputum. Patients with smear-positive disease are considered to be infectious until they have been treated for at least 2 weeks¹⁰. ‘Smear-negative’ or ‘closed’ TB is pulmonary disease in which AFBs are

Key Points

Suspect TB in all patients with a persistent cough, chronic chest problems or the systemic symptoms of fever, night sweats and/or weight loss

All cases of TB should be referred to a recognised TB specialist

Make certain that specimens are sent to the TB reference laboratory for culture, and remind surgeons to send fresh samples to microbiology

Ensure that local TB control programmes are adequately funded and staffed

TB is a global problem: ensure that Western governments support the TB programmes of poorer developing nations

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not seen on initial inspection but are later grown and identified in the culture laboratory. Together with patients with non-pulmonary disease, smear-negative patients are usually considered non-infectious.

Epidemiology of TB in the UK

In the year 2000, 7325 cases of TB were notified in the UK; 2938 of these were in London. This represents a national increase of 10% over the previous year, and a rise of 20% in the capital. Approximately 8% of the cases were isoniazid resistant; MDR TB accounts for about 1% of the notifications, with half of the cases occurring in London^{1,6,11-13}.

Many cases occur in 'clusters'; a large cluster may be termed an outbreak, the Leicester community college outbreak being an unusually large one. The most recent published figures for the Leicester outbreak show that 67 of the 1208 pupils at the school have been diagnosed with active tuberculosis, together with two teachers and six family members of students; 246 pupils had a strongly positive Heaf test, implying infection but not active disease, and have been offered chemoprophylaxis. Isolates of *Mycobacterium tuberculosis* obtained so far have been fully sensitive to antituberculous medication. The investigation of the outbreak in Leicester revealed other cases within the community that are thought to be unrelated to the main outbreak¹⁴. In Wandsworth, where the index patient was a teacher, three young children were treated for active disease and 16 were offered chemoprophylaxis¹⁵. Eight pupils were given full treatment in Newport, while many others were screened¹⁶.

Professional awareness of TB

Tuberculosis is not simply a historical disease and is by no means uncommon in the UK. This needs to be remembered when dealing with patients who are not in a classical 'high-risk' group. Every patient with a persistent cough or a chronic chest condition should be investigated for TB, together with those with unexplained weight loss or fevers. Sputum samples sent for microbiological culture are not automatically processed for Ziehl-Nielsen staining and TB culture, and it is important that both GPs and hospital practitioners are aware of this. Some medical professionals, working in areas with a low incidence of TB and many years out of medical school, may be only vaguely aware that TB is not just a pulmonary disease but can occur in any organ of the body, including the brain, bone and lymph nodes. It is equally important to educate our surgical colleagues to send part of their specimens fresh, not fixed in formalin, to the microbiology department for culture if there is any suspicion of TB. Single-drug resistance can rapidly become multi-drug resistance on inadequate therapy.

Public awareness

Public education is crucial. There is a problem with both awareness that TB is present in the UK and the degree of understanding of the disease, even in communities with high rates of

TB. Fifty years ago, most of the adult lay public in the UK could have made a diagnosis of TB when they or a relative had typical symptoms. In my work amongst the Bangladeshi community of East London, a relatively high-risk group for TB, I have noted a marked lack of understanding about the disease. Cough and haemoptysis are often associated with ill health, including TB, and necessitate a medical consultation. However, symptoms such as fever, night sweats and weight loss can be attributed to a cold, a 'flu-like illness, stress or overwork. A number of patients with both pulmonary and extrapulmonary disease dismissed their protracted history of daily high temperatures, and some consulted traditional healers for a remedy¹⁷. In a recent audit of spinal tuberculous infection in the same area, I found that many of the patients had had systemic symptoms of night sweats, fever and weight loss for up to a year before the diagnosis was finally made¹⁷.

Social stigma is linked to the public's understanding of the disease. For many young people from Asian communities a diagnosis of TB is tantamount to a social death sentence. Their prospects of a 'good marriage' may diminish sharply. This fear is not a problem only in the Indian subcontinent, where women have been reported to be divorced or thrown out of their marital homes if diagnosed with the disease, it is a problem in the UK as well^{17,18}. Many people still believe that TB is an inherited disease, and that a family cluster of cases is transmitted through the genes rather than by droplet infection¹⁷. Considerable reassurance and health education is still needed to relieve unnecessary and distorted fears about the disease.

The national TB control programme

Outbreaks such as those in Leicester, Wandsworth and Newport not only highlight the lack of professional and public knowledge about TB but also emphasise the importance of adequately funded and appropriately staffed TB control programmes. In the UK over the past few years, there has been a lack of specialist TB nurses, a suspension of the Bacille-Calmette-Guérin (BCG) immunisation programme due to manufacturing problems¹⁹ and shortages of both isoniazid and streptomycin.

For every 50 cases of TB per year, there should be one full-time specialist nurse. Unfortunately, even in some of the high-incidence areas of the UK, such staffing levels are still to be achieved¹⁰. Specialist nurses not only monitor TB treatment and support patients but also organise contact tracing. Generally, 10% of TB cases are picked up through screening close contacts of the index patient⁸. Considerably more cases were found by screening in the recent outbreaks.

Local programmes also coordinate new-entrant screening with referrals from national airports and seaports. Supervision of directly observed therapy (DOT) for patients who find it difficult to adhere to their drug regimes, for whatever reason, is also an important role for specialist nurses. However, in some areas, this level of treatment monitoring is difficult to introduce when human resources are lacking.

Department of Health guidelines require respiratory or infectious-disease specialists to oversee all cases of TB, regardless of

the site of disease²⁰. In many cases, the joint skills of a recognised 'TB physician' and surgical colleague optimise patient management. Inadequate treatment and patients' lack of adherence to medication promote the development of resistant strains. Supervision of MDR TB is even more crucial, and should be undertaken in only a few specialist centres in the UK.

The schools BCG immunisation programme was resumed in September 2001. The high rates of disease in the Leicester outbreak, however, are not thought to have been due to the programme's interruption, as many of the pupils would have received neonatal BCG¹⁹.

The international climate

While concerned about the situation in the UK, we should remember that 95% of cases of TB worldwide occur in developing countries; what we see in Western Europe and North America is the tip of the iceberg in terms of the global distribution of the disease²¹.

The World Health Organisation declared TB a 'global health emergency' in 1993, and set out to promote a worldwide programme of directly observed therapy – short course (DOTS). Its goals are to reduce TB morbidity and deaths by promoting the worldwide use of DOTS and other effective TB control strategies, and to assess existing strategies and develop new strategies for the prevention and control of TB through operational, epidemiological and economic research²².

DOTS has five key components²²:

- government commitment to sustained TB control activities
- case detection by sputum-smear microscopy of symptomatic patients self-reporting to health services
- a standardised treatment regimen lasting 6–8 months for at least all sputum-smear-positive cases, with DOT for at least the initial 2 months
- a regular uninterrupted supply of all essential anti-TB drugs
- a standardised recording and reporting system that allows assessment of treatment results for each patient and for the TB control programme overall.

DOTS is now operating in 127 countries worldwide. However, it is only as effective as the local infrastructure that supports it: the supply of antituberculous drugs in many places remains sporadic, leaving patients without therapy for weeks or even months. In rural areas, patients may have to travel long distances to reach their nearest clinic, and bad weather and/or poor transport systems may prevent health workers from visiting isolated villages. War and civil disturbances also disrupt health services.

Funding, of course, is also a major factor. For medical personnel to be both motivated and clinically effective they need to be appropriately paid. Equipment, transport and administration all cost money. However, it has been estimated that half the world's population live in countries where the annual health budget is less than US\$10 per capita²³. Without financial support from richer industrialised countries, these areas cannot possibly maintain TB treatment programmes.

MDR TB

Multi-drug-resistant tuberculosis (MDR TB) is defined as *in vitro* resistance to both isoniazid and rifampicin, with or without resistance to other anti-TB drugs²⁴. Resistance may be primary or acquired. Primary resistance refers to MDR TB that occurs in an individual who has not been previously treated for TB and has, therefore, been infected by an index patient with the disease. Acquired resistance, seen in the majority of MDR TB cases in the UK, occurs in patients who have previously been treated for drug-sensitive disease for at least a month.

A recent survey by the World Health Organisation and the International Union Against Tuberculosis and Lung Disease revealed alarmingly high rates of MDR TB in some areas. While Western Europe had a combined (primary and acquired disease) prevalence of MDR TB of less than 1% of all TB cases, the same figures for Latvia and Estonia were 22.1% and 11.7%, respectively. In the Americas, the Dominican Republic had a combined rate of 8.6%, and in Argentina the figure was 8%. The Delhi region of India had an MDR TB prevalence of 13.3%, and in Sierra Leone, in sub-Saharan Africa, it was 4.2%²⁵.

Although the number of cases in the UK is not large, approximately 40–50 cases annually¹³, the medical problems associated with the disease, as well as the social and resource implications, are significant. Patients often require isolation in negative-pressure rooms for many months. They can become social outcasts, particularly amongst the immunocompromised community, because of others' fears of catching the infection. Some of the third-line TB drugs have neurological and psychological side effects, and the isolation experience can also cause depression and psychosis. In a recent study, the average drug cost of treating a case of MDR TB was estimated at £10,000 (sensitive disease costs approximately £120 for 6 months' treatment), while the total cost of care topped £60,000²⁶. One multi-institutional outbreak of MDR TB in New York City was estimated to have cost at least US\$ 25 million for inpatient hospital stays alone⁷, while another US\$ 1 billion was spent on public-health measures to curtail the spread of the disease²⁷.

If these costs are reflected in even basic treatment plans for patients in developing countries and in countries with an inadequate healthcare infrastructure, then most people with MDR TB in these countries are unlikely to receive appropriate therapy. In some areas, where there are no reliable culture facilities, patients are assumed to have MDR TB if they remain smear positive after several courses of standard therapy. If they are lucky and the resources are available they are put on a 'best-guess' regime of the locally available second- and third-line anti-tuberculous drugs.

In conclusion

Whether in Europe, North America or a developing country, TB control programmes rely on well-informed well-supported medical personnel, together with adequate funding to finance the staff, hospital care, medication, microbiological facilities and administration required during treatment. It is also essential

that the general population is accurately informed about the disease and knows where to seek treatment and advice. Rates of MDR TB are on the increase, while many countries do not even have the health infrastructure adequately to manage sensitive strains of the disease.

The tone of this article may sound both political and philanthropic. However, adequate staffing levels and funding in health-care are potent political issues. Likewise, we are a global society, with enormous amounts of international travel and migration. The TB bacillus needs no passport, and an epidemic of MDR TB would not stop at international borders. A lack of philanthropic gestures by wealthy countries now could emerge as an international health disaster in the future, with consequences for us all.

We may have lost the chance over the last 50 years to control and possibly even eradicate TB, but we should learn from the experience. Both national and international efforts to control the infection should be wholeheartedly embraced, and we should not miss the opportunity to conquer the disease in the twenty-first century.

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